

- A method for assaying a candidate compound for its ability to interact with a modified receptor tyrosine kinase (RTK) polypeptide comprising:
 - a) expressing an isolated DNA sequence or variants thereof encoding the modified RTK gene construct wherein said RTK gene contains a synthetic catalytic linker wherein said linker comprises at least one amino acid from the kinase insert domain (KID) of the VEGFR-2 gene catalytic region, in a host capable of producing a form of the polypeptide which form may be assayed for interaction of said polypeptide with said candidate substance;
 - b) exposing said modified polypeptide to said candidate substance; and
 - c) evaluating the interaction of said polypeptide with said candidate substance.
- 2. The method of claim 1, wherein said evaluation step further comprises:
 - (a) crystallizing said modified polypeptide in a condition suitable for x-ray crystallography; and
 - (b) conducting said x-ray crystallography on said polypeptide.
- 3. A method for assaying a candidate compound for its ability to interact with a modified VEGFR-2 receptor polypeptide comprising:
 - a) expressing an isolated DNA sequence or variants thereof encoding the modified VEGFR-2 gene construct wherein said VEGFR-2 gene contains a synthetic catalytic linker wherein said linker comprises at least one amino acid from the kinase insert domain (KID) of the VEGFR-2 gene catalytic region, in a host capable of producing a form of the polypeptide which form may be assayed for interaction of said polypeptide with said candidate substance;
 - b) exposing said modified polypeptide to said candidate substance; and
 - c) evaluating the interaction of said modified polypeptide with said candidate substance.
- 4. The method of claim 2, wherein said evaluation step further comprises:

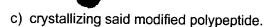




- (a) crystallizing said modified polypeptide in a condition suitable for x-ray crystallography; and
- (b) conducting said x-ray crystallography on said polypeptide.
- 5. An isolated DNA sequence or variants thereof encoding a modified RTK gene construct wherein said RTK gene contains a synthetic catalytic linker wherein said linker comprises at least one amino acid from the kinase insert domain of the RTK gene catalytic region.
- 6. An isolated DNA sequence or variants thereof encoding a modified VEGFR-2 gene construct wherein said VEGFR-2 gene contains a synthetic catalytic linker wherein said linker comprises at least one amino acid from the kinase insert domain of the VEGFR-2 gene catalytic region.
- 7. The isolated oligonucleotide sequence of claim 6 comprising a DNA sequence or variants thereof in SEQ. ID NO. 5.
- 8. The isolated oligonucleotide sequence of claim 6 comprising a DNA sequence or variants thereof in SEQ. ID NO. 6.
- 9. A method of assessing compounds which are agonists or antagonists of the activity of the a modified RTK gene polypeptide wherein said modified RTK gene contains a synthetic catalytic linker wherein said linker contains at least one amino acid from the kinase insert domain of the RTK polypeptide catalytic region comprising:
 - a) crystallizing said modified RTK polypeptide;
 - b) obtaining crystallography coordinates for said crystallized modified RTK polypeptide;
 - c) applying said crystallography coordinates for said modified RTK polypeptide to a computer algorithm such that said algorithm will generate a model of said RTK polypeptide suitable for use in designing molecules that will act as agonists or antagonists to said polypeptide; and
 - d) applying and iterative process whereby various molecular structures are applied to said computer generated model to identify potential agonists or antagonists to said



- 10. A method of assessing compounds which are agonists or antagonists of the activity of the a modified VEGFR-2 gene polypeptide wherein said modified VEGFR-2 gene contains a synthetic catalytic linker wherein said linker comprises at least one amino acid from the kinase insert domain of the VEGFR-2 polypeptide catalytic region comprising:
 - a) crystallizing said modified VEGFR-2 polypeptide;
 - b) obtaining crystallography coordinates for said crystallized modified VEGFR-2 polypeptide;
 - c) applying said crystallography coordinates for said modified VEGFR-2 polypeptide to a computer algorithm such that said algorithm will generate a model of said VEGFR-2 polypeptide suitable for use in designing molecules that will act as agonists or antagonists to said polypeptide; and
 - d) applying and iterative process whereby various molecular structures are applied to said computer generated model to identify potential agonists or antagonists to said polypeptide.
 - 11. The method of claim 10, wherein said modified VEGFR-2 polypeptide comprises the VEGFR2Δ50 polypeptide of Seq. ID No. 5.
 - 12. An isolated DNA sequence comprising a DNA sequence or variants thereof encoding the VEGFR-2 gene construct having the x-ray coordinates of Figure 5.
 - 13. A method for preparing proteins or polypeptides of the receptor tyrosine kinase family such that they are suitable for measurement by x-ray crystallography comprising:
 - a) identification of the Kinase Insert Domain within the catalytic domain of said proteins;
 - b) deletion of a specific number of amino acid residues from said Kinase Insert Domain such that the modified polypeptide now has a stable conformation such that it may form a crystalline state suitable for being measured by x-ray crystallography; and



- 14. A process of drug design for compounds which interact with RTK polypeptides comprising:
 - a) deletion of a portion of the KID of the target RTK polypeptide;
 - b) crystallizing said target RTK polypeptide;
 - c) resolving the x-ray crystallography of said target RTK polypeptide;
 - d) applying the data generated from resolving the x-ray crystallography of said target RTK polypeptide to a computer algorithm which will generate a model of said target RTK polypeptide suitable for use in designing molecules that will act as agonists or antagonists to said polypeptide; and
 - e) applying an iterative process whereby various molecular structures are applied to said computer generated model to identify potential agonists or antagonists to said target RTK polypeptide.
- 15. A process of drug design for compounds which interact with modified VEGFR-2 polypeptides comprising:
 - a) deletion of a portion of the KID of the modified VEGFR-2 polypeptide;
 - b) crystallizing said modified VEGFR-2 polypeptide;
 - c) resolving the x-ray crystallography of said modified VEGFR-2 polypeptide;
 - d) applying the data generated from resolving the x-ray crystallography of said modified VEGFR-2 polypeptide to a computer algorithm which will generate a model of said modified VEGFR-2 polypeptide suitable for use in designing molecules that will act as agonists or antagonists to said polypeptide; and
 - e) applying an iterative process whereby various molecular structures are applied to said computer generated model to identify potential agonists or antagonists to said modified



